



# Armed Forces College of Medicine

## AFCM



# Treatment of Osteoporosis

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## INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture you will be able to:

1. Classify drugs used in the treatment of osteoporosis
2. Describe pharmacokinetics, mechanism of action and adverse effects of drugs used in the treatment of osteoporosis

# **Definition**

- **Osteoporosis** is a condition of skeletal fragility due to progressive loss of bone mass.

- **Occurrence:**

- It occurs in elderly people of both sexes but is most pronounced in postmenopausal women.
- Osteoporosis is characterized by frequent bone fractures, which are a major cause of disability among elderly people.

- **Nondrug strategies to reduce bone loss in postmenopausal women include:**

1. A diet adequate in calcium and vitamin D,
2. Weight-bearing exercise,
3. Cessation of smoking
4. Patients at risk for osteoporosis should avoid drugs that increase bone loss such as glucocorticoids.

# **Drugs used to treat osteoporosis**

- 1.Bisphosphonates**
- 2.Selective estrogen-receptor modulator**
- 3.Calcitonin**
- 4.Teriparatide**
- 5.Denosumab**

## I) Bisphosphonates

1. Alendronate,
2. Risedronate,
3. Ibandronate,
4. Zoledronic acid have been approved for the **prevention** and **treatment** of osteoporosis.

• The **bisphosphonates** decrease osteoclastic bone resorption via several mechanisms, :

1. Decrease in osteoclastic formation/activation,
2. Increase in osteoclastic apoptosis (programmed cell death), and
3. Inhibition of the cholesterol biosynthetic pathway important for osteoclast function.

- The decrease in osteoclastic bone resorption results in a small but significant net gain in bone mass in osteoporotic patients, because the bone-forming osteoblasts are not inhibited.
- Treatment with bisphosphonates decreases the risk of bone fracture in patients with osteoporosis.

## **1. Pharmacokinetics:**

- ***Alendronate, risedronate, and ibandronate:***

Orally active agents for osteoporosis, although less than 1 % of the administered dose is absorbed.

- **Alendronate and risedronate** may be dosed once daily or once weekly.
- **Risedronate** is also available in a once monthly oral dosage form.
- Food significantly interferes with absorption of oral bisphosphonates.
- **VIP** Bisphosphonates should be administered with 1 litre of plain water at least 30 minutes (60 minutes for *ibandronate*) before eating breakfast or taking other medications. Patient should stay in upright position for 30 min **to minimize oesophageal irritation**

- Elimination from the body is primarily through **renal clearance**, and the **bisphosphonates should not be given to individuals with severe renal impairment.**
- For patients **unable to tolerate oral bisphosphonates**, **intravenous *ibandronate* and *zoledronic acid*** are **alternative treatments for osteoporosis.**

## **2. Adverse effects:**

- Diarrhea, abdominal pain, and musculoskeletal pain.
- ***Alendronate, risedronate, and ibandronate*** are associated with **esophagitis and esophageal ulcers.**
- **VIP** To minimize the risk of esophageal irritation, patients should remain upright for at least 30 minutes (60 minutes for *ibandronate*) after taking a bisphosphonate.
- **Osteonecrosis of the jaw** has been reported with bisphosphonates.
- ***Etidronate*** is the **only member** of the class that **causes osteomalacia** following long-term.

## **II) Selective estrogen-receptor modulators**

- Estrogen replacement is an effective therapy for the prevention of postmenopausal bone loss.
- When initiated in the immediate postmenopausal period, estrogen therapy prevents osteoporosis and reduces the risk of hip fracture.
- [Note: Estrogen-progestogen therapy is no longer the therapy of choice for the treatment of osteoporosis in postmenopausal women because of increased risk of

# Raloxifene

- *Raloxifene* is a selective estrogen-receptor modulator approved for the prevention and treatment of osteoporosis.
- It increases bone density without increasing the risk of endometrial cancer.
- *Raloxifene* is a first-line alternative for postmenopausal osteoporosis in women who are intolerant to bisphosphonates.

### **III) Calcitonin (Serum calcium lowering hormone)**

- *Calcitonin*, administered **intranasally**, is effective and well tolerated in the treatment of postmenopausal osteoporosis.
- The drug reduces bone resorption, but it is less effective than the bisphosphonates.
- A **special property of calcitonin is the relief of pain** associated with osteoporotic fracture. Therefore, *calcitonin* may be beneficial in patients who have recently suffered a vertebral fracture.

### **III) Calcitonin (Serum calcium lowering hormone)**

#### **Common adverse effects:**

- The intranasal formulation include rhinitis and other nasal symptoms.

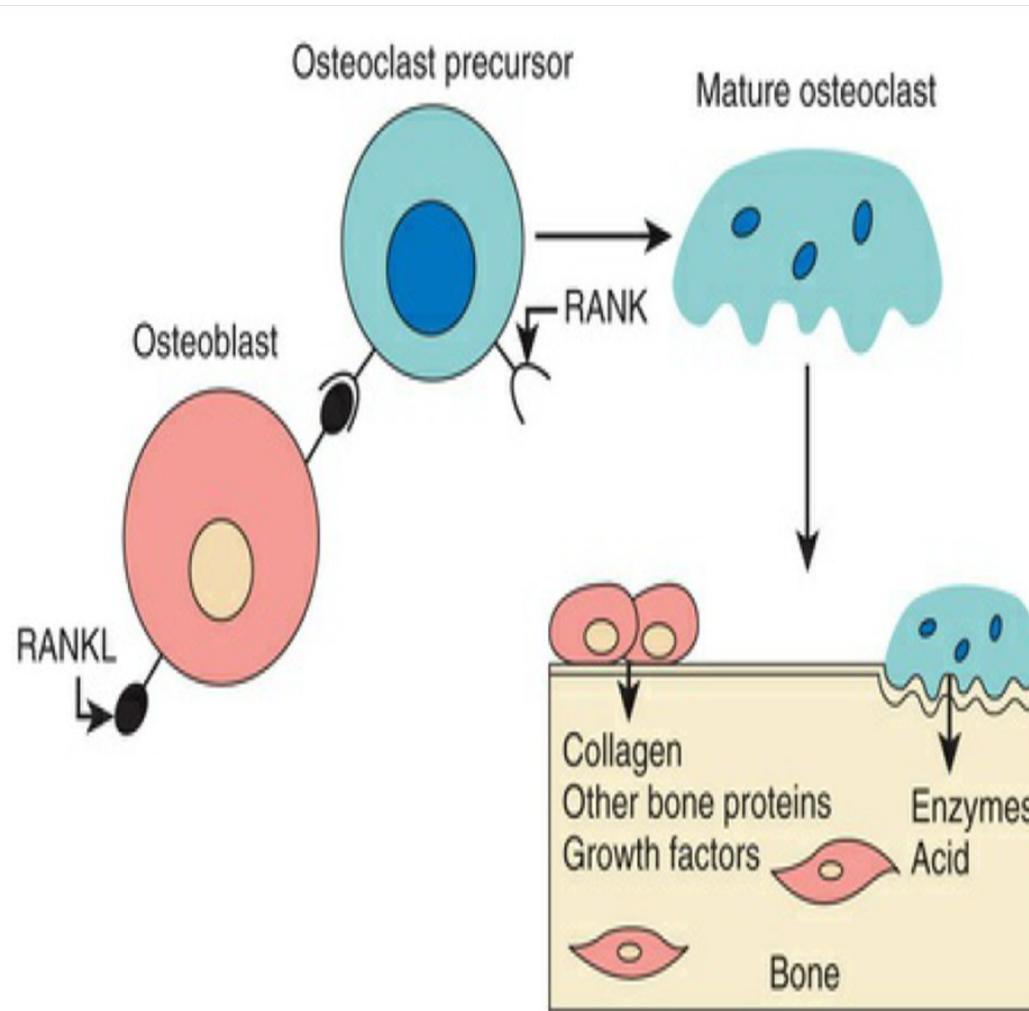
**A parenteral formulation** of *calcitonin* is available for intramuscular or subcutaneous injection, but it is infrequently used in the treatment of osteoporosis.

## IV) Teriparatide

- *Teriparatide* is a **recombinant segment of human parathyroid hormone** that is administered **subcutaneously** for the treatment of osteoporosis.
- Parathyroid hormone given continuously leads to dissolution of bone. However, when it is given subcutaneously once daily, bone formation is the predominant effect by preferentially stimulating osteoblastic activity over osteoclastic activity.

## V) Denosumab

- *Denosumab* is a **monoclonal antibody** that **targets receptor activator of nuclear factor kappa - B ligand (RANKL)** and **blocks osteoclast activation.**



**Bone Remodeling and the Roles of Osteoblast and Osteoclast Proteins.** Osteoclast precursors express receptors (RANK) that interact with the osteoblast membrane-associated cytokine, RANKL. This interaction leads to osteoclast maturation and the formation of a ruffled membrane, promoting binding to the bony surface and accompanied by protein degradation, acidification, and bone

## V) Denosumab

- *Denosumab* is approved for treatment of **postmenopausal osteoporosis in women at high risk of fracture.**
- It is administered via **SC injection every 6 months.**

## V) Denosumab

### **Adverse effects :**

- Increased risk of infections, secondary malignancies, hypocalcemia, and dermatological reactions.
- It should be **reserved for women intolerant of or unresponsive** to other osteoporosis therapies.



## SUGGESTED TEXTBOOKS

1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7<sup>th</sup> edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14<sup>th</sup> edition) New York: McGraw-Hill Medical.

# *Thank You*